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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,708	06/12/2001	Se-Jin Lee	JHU1320-4	7387

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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/27/2003

/D

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/880,708	LEE ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on th cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-14* is/are pending in the application.

4a) Of the above claim(s) *9,10,13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8,11,12 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *2-14* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1 1/2* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 2-14 are pending.

Applicant's election with traverse of the detectable label species and a fluorescent compound species of detectable label in Paper No. 9 is acknowledged. The traversal is on the ground(s) that anti-GDF-5 antibodies are novel and therefore there is no need to limit the search to a particular species, a search of haptens overlaps that of fluorescent compounds, there is a commonality of operation, function or effect of the species of detectable label and therefore they should be examined together. This is not found persuasive because the examiner has not determined that the invention is allowable, each of the species is independent and distinct, wherein each is not required for the other and each can be used and manufactured independently and further each requires a separate search, although species may share a commonality of operation, function or effect this is not an indication for examination of all species claimed no more than the fact all proteins share a commonality of operation, function or effect in that they all can operate, function, or effect as molecular weight markers and therefore every conceivable polypeptide that applicant could claim should be examined together, especially in the case wherein each is not required for the other and each can be used and manufactured independently and further each requires a separate search, Applicants' arguments regarding a fluorescent compound and fluorescein says nothing regarding the distinctness of the other species.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9, 10, 13, 14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

The application is not fully in compliance with the sequence rules, 37 C.F.R. § 1.821-1.825. Specifically, the specification fails to recite the appropriate sequence identifiers at each place where a sequence is discussed. See Figures 2 and 3. This is not meant to be an exhaustive list of places where the specification fails to comply with the sequence rules. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. The application cannot issue until it is in compliance. Nucleic acid sequences with 10 or more nucleotides, at least 4 of which are specifically defined, must comply with the sequence rules. Amino acid sequences with 4 or more residues, at least 4 of which are specifically defined, must comply with the sequence rules. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the "Sequence Listing." Applicant may bring the figure(s) into compliance by amending either the figure(s) or the "Brief Description of the Drawings" to recite the appropriate sequence identifier.

Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-8, 11, 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting GDF-5 comprising the amino acid sequence shown in figure 2, does not reasonably provide enablement for a method of detecting a cell proliferative disorder by detecting GDF5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are directed to or encompass detecting any and/or all cell proliferative disorders or a uterine neoplasm, endometriosis, or a skeletal disorder by detecting GDF5. However, the claims do not set forth the steps in the detection of disorder or whether an increase or decrease in GDF5 is associated with a cell proliferative disorder. There is nothing in the present specification or prior art of record suggesting that GDF-5 is associated with any and/or all cell proliferative disorders. The detection of GDF5 transcripts in embryonic tissue or the control of particular aspects of skeletal morphology during development is not predictive of cell proliferative disorders in an adult because many cytokines that subserve familiar functions postnatally play different or unknown roles embryologically and given the amino acid sequence of a cytokine and any of its actions one cannot predict when or where it will do what else. See Nathan (u10), page 981, paragraph bridging columns 1-2. TGF-β1 stimulates the growth of fibroblasts from very early human fetuses, but inhibits the growth of fibroblasts derived from fetuses of somewhat later gestational

age. See Hill (v10), Abstract. Accordingly, there is a lack of predictability in the art. The specification lacks guidance for, and working examples of, the detection of any and/or all cell proliferative disorders or a uterine neoplasm, endometriosis, or a skeletal disorder. The specification lacks guidance for, and working examples of, subjects suspected of having a GDF5 associated disorder. The skilled is left to an undue amount of unduly extensive, random, trial and error experimentation in order to determine how to achieve such detection. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

Claims 2-8, 11, 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for GDF5 comprising the amino acid sequence shown in Figure 2, does not reasonably provide enablement for GDF5 without regard to the structure thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification intends the term "GDF-5" to encompass polypeptides produced by minor modifications of GDF-5, and which have substantially equivalent activity to GDF-5. Such modifications may be deliberate or spontaneous (page 10, lines 1-10). The specification teaches that GDF-5 is capable of inducing bone formation in vivo (page 29, full paragraph 2). The specification envisions using antibodies that bind GDF-5 for the detection, diagnosis, or therapy of GDF-5-related disorders (paragraph bridging pages 15-16). However,

the instant specification does not identify those amino acid residues in the amino acid sequence of a GDF-5 which are essential for its antigenicity and those residues which are either expendable or substitutable. In the absence of this information a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis of over 495 amino acid residues before they could even begin to rationally design an antibody that binds to a GDF-5 having other than a natural amino acid sequence. Furthermore, the prediction of antigenic epitopes is unpredictable. See Daniel (AE, cited by Applicants) wherein it is taught that approaches to predicting antigenic epitopes based on primary amino acid sequence data were unsuccessful. Furthermore, these same approaches were unsuccessful at predicting known antigenic epitopes. Still further the antigenicity of any particular peptide was dependent upon the carrier (page 540, Abstract). Accordingly, it appears that a large number of the embodiments encompassed by antibodies that bind to a GDF-5 polypeptide identified by name only would not bind to a GDF-5 polypeptide having the natural sequence and the specification has not taught one skilled in the art how to use an antibody that does not bind to a GDF-5 polypeptide having the natural sequence for the detection, diagnosis, or therapy of GDF-5-related disorders. In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and use the full scope of the claimed invention.

Claims 2-8, 11, 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to or encompass antibodies that bind GDF5. The specification intends the term "GDF-5" to encompass polypeptides produced by minor modifications of GDF-5, and which have substantially equivalent activity to GDF-5. Such modifications may be deliberate or spontaneous (page 10, lines 1-10). GDF is a genus The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to GDF5. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, GDF5 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus and the antibodies thereto.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following claims are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-8, 11, 12 are indefinite because they recite the term "GDF5". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "GDF5" an artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claim 14 recites the limitation "the solid phase carrier" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 14 is indefinite because it recites the term "modified cellulose". Because the instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "modified cellulose" an artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The nature and extent of the modification are not clearly set forth. The metes and bounds are not clearly set forth.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

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ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
JANUARY 26, 2003